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Abstract
Iron porphryin complexes are active catalysts for the cyclopropanation of alkenes by ethyl diazoacetate. Fe(TIP) (TIP = meso-tetra-p-tolylporphyrin), an isolated iron(II) porphyrin complex, can be used as the catalyst, or the iron(III) complexes of several porphyrins can be reduced in situ. The reactions produce synthetically useful excesses of the trans cyclopropyl ester products. This stereoselectivity exhibits a modest solvent dependence, with donor solvents giving higher ratios of the trans cyclopropane products. The diastereoselectivity exhibits only a modest dependence on the steric bulk of the porphyrin. The reactions are selective for 1-alkenes and 1, 1-disubstituted alkenes. Conjugated substrates and enol ethers react more rapidly than simple aliphatic alkenes. A mechanistic model for the iron-mediated reactions is proposed which is consistent with the data presented herein.

Disciplines
Chemistry

Shape and Stereoselective Cyclopropanation of Alkenes Catalyzed by Iron Porphyrins

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Abstract: Iron porphryin complexes are active catalysts for the cyclopropanation of alkenes by ethyl diazoacetate. Fe(TTP) (TTP = *meso*-tetra-*p*-tolylporphyrin), an isolated iron(II) porphyrin complex, can be used as the catalyst, or the iron(III) complexes of several porphyrins can be reduced in situ. The reactions produce synthetically useful excesses of the trans cyclopropyl ester products. This stereoselectivity exhibits a modest solvent dependence, with donor solvents giving higher ratios of the trans cyclopropane products. The diastereoselectivity exhibits only a modest dependence on the steric bulk of the porphyrin. The reactions are selective for 1-alkenes and 1,1-disubstituted alkenes. Conjugated substrates and enol ethers react more rapidly than simple aliphatic alkenes. A mechanistic model for the iron-mediated reactions is proposed which is consistent with the data presented herein.

The metal-catalyzed cyclopropanation of substituted olefins by diazo esters is a reaction commonly employed in organic synthesis.[1] Chiral copper[2−4] and rhodium[5,6] catalysts have recently been reported to effect cyclopropanation with high enantioselectivity. However, the diastereoselectivities obtained in these reactions are generally poor. Mixtures of the trans and cis cyclopropyl esters are produced, with the trans isomer obtained in only a slight excess. A notable exception is a recently reported ruthenium catalyst,[7] which provided high enantioselectivities and trans/cis ratios of 10:1 using ethyl diazoacetate (EDA) as the carbene source.

We are interested in the development of metalloporphyrin cyclopropanation catalysts, since such reactions often exhibit unique stereoselectivities and exceedingly high catalyst turnover numbers. For example, rhodium(III) porphyrin-catalyzed cyclopropanation reactions using EDA as the carbene source produced the cis cyclopropyl ester as the major product when bulky ligands such as the tetramesitylporphyrin (TMP) (see Figure 1) were employed.[8−11] To the best of our knowledge, this is the only example of a catalyst that produces synthetically useful excesses of cis cyclopropyl esters.

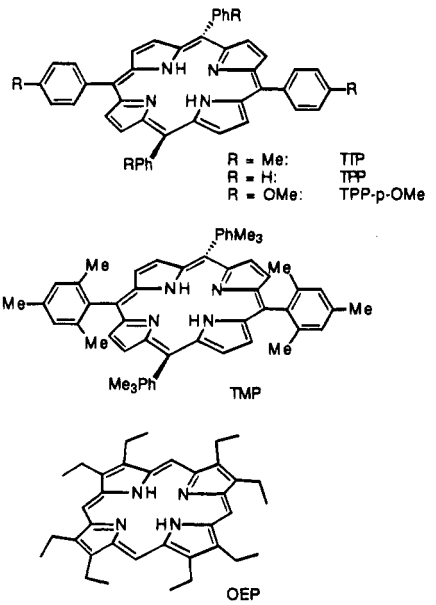

Figure 1. Structures of the porphyrins used in this study.

More recently, osmium(II) porphyrins have been shown to catalyze the cyclopropanation of alkenes with diazoesters. These reactions also exhibit good diastereoselectivity, but of the opposite sense. Using styrene as the substrate and EDA as the carbene source, catalysts such as the osmium(II) tetra-*p*-tolylporphyrin (TTP) dimer, (TTP)Os(pyridine)$_2$, and (TTP)-Os(CO)(pyridine) provided the trans product in up to a 10-fold excess over the cis cyclopropyl ester.[12,13] The divergent stereoselectivities observed in these reactions are curious, since investigations of stoichiometric osmium and rhodium porphyrin-catalyzed cyclopropanation reactions have suggested that the active species are the isoelectronic Os(II) and Rh(III) carbenes, respectively. Thus, it would appear that subtle factors have a profound effect on the stereochemical outcome of the reaction with these two metals.

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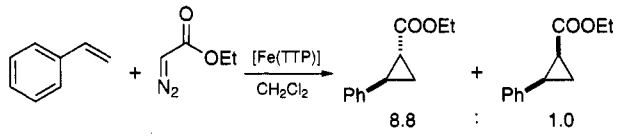
In this paper, we describe studies of iron porphyrin-catalyzed alkene cyclopropanations. First, we hoped that the analysis of a third type of porphyrin catalyst would shed light on the unusual metal dependence of the product stereochemistry. Second, while the osmium and rhodium porphyrins and the ruthenium tripyridyl complex are efficient catalysts, they are expensive and are not currently commercially available. If an efficient and stereoselective catalyst containing a more inexpensive metal could be devised, this might be more practical for use in large-scale organic synthesis. We find that iron porphyrins are excellent catalysts for the cyclopropanation of some alkenes by diazoesters. The reactions produce synthetically useful excesses of the trans cyclopropyl ester. The iron porphyrin catalysts exhibit pronounced substrate selectivities that may be useful in the selective cyclopropanation of polyolefins. A model for carbene transfer from the metal to the alkene is proposed that is consistent with all of the data regarding porphyrin-based catalysts reported to date. This model will be of great utility in designing chiral metalloporphyrins for asymmetric cyclopropanation reactions.

Results

Iron(II) Porphyrins Catalyze the Cyclopropanation of Styrene. Iron(II) porphyrins are isoelectronic with osmium(II) and rhodium(III) porphyrins and so were examined for cyclopropanation activity. It was found that Fe^{II}(TTP) was quite active in the presence of styrene and EDA. Approximately 1300 catalyst turnovers were observed over an hour and an 8.8 to 1 ratio of trans to cis cyclopropyl esters was produced, comparable to the best results obtained with other types of catalysts. This trans-selective reaction appears to be more closely related to the osmium-catalyzed process than the rhodium-mediated reaction and suggests that for the iron triad, the transition state for carbene transfer favors the thermodynamically more stable stereochemical arrangement of the ester and the alkene substituent.



In Situ Reduction of Iron(III) Porphyrins Provides Highly Active Cyclopropanation Catalysts. Given this encouraging result, we wished to examine the scope of the iron porphyrin-catalyzed cyclopropanation reaction. However, because of their air-sensitivity, isolated iron(II) porphyrins are easily handled only in an inert atmosphere box and are generally not convenient reagents for organic synthesis. In order to devise a more practical process, we examined the *in situ* reduction of air-stable iron(III) porphyrins under argon as a means to generate an active catalyst. Since EDA is known to be a mild reducing agent,[14] we mixed the chloroiron(III) derivative of tetraphenylporphyrin (TPP) with styrene and EDA in dichloromethane. Neither the production of cyclopropanes nor the decomposition of EDA was observed at room temperature. However, heating the solution to reflux was sufficient to initiate a reaction that was dependent on the presence of the catalyst. The ratio of stereoisomeric products was 5.5:1 with the trans cyclopropyl ester predominating. When the argon blanket was removed, the reaction proceeded very sluggishly. This supports the contention that the active species is the air-sensitive iron(II) porphyrin.

Since it seemed likely that higher stereoselectivities would be obtained at reduced temperatures, we explored other protocols for the *in situ* reduction of iron(III) porphyrins. It was found that the one-electron reductant cobaltocene is a superior reagent for this purpose. In the presence of cobaltocene and the Fe(TPP)Cl precatalyst, the reaction proceeded to completion in a short period of time and excellent turnover numbers were observed. For example, more than 900 equiv of styrene with respect to catalyst were cyclopropanated in 2 h at room temperature. The diastereoselectivity was identical, within experimental error, to that observed using preformed Fe^{II}TTP (8.7 to 1 ratio of trans to cis cyclopropanes). Although cobaltocene itself is air-sensitive, its oxidation is very slow and reactions can be set up conveniently without the use of a glovebox. Cobaltocene alone also mediated cyclopropanation under these conditions, but the rate was so low that this reaction did not contribute significantly to product accumulation and had no effect on the stereochemical outcome. For example, only four turnovers per cobalt in a 4-h period were observed when cobaltocene alone was used to catalyze the cyclopropanation of *p*-methoxystyrene.

Influence of Porphyrin Structure and Solvent on Product Stereochemistry. Using this more convenient system, we explored the effect of changing the peripheral substituents on the porphyrin ligand. In rhodium porphyrin-catalyzed cyclopropanations, bulkier, more bowl-shaped ligands provide higher ratios of cis to trans cyclopropyl ester products. However, as shown in Table 1, a variety of porphyrins with very different steric environments around the catalytic iron atom produced similar ratios of cyclopropyl ester stereoisomers. For example, in the iron-catalyzed reaction between EDA and styrene, the crowded tetramesitylporphyrin (TMP) ligand and the unencumbered octaethylporphyrin (OEP) ligand (Figure 1) supported reactions that provided 13:1 and 10:1 ratios of trans to cis cyclopropyl esters, respectively. This modest difference was not part of a trend. The TTP ligand, which is intermediate in bulk between the OEP and TMP ligands, supported a product ratio of 8.8 to 1. The addition of an electron-donating *p*-methoxy group to the porphyrin arene rings also had essentially no effect. We conclude that the substrate and the porphyrin substituents do not interact significantly.

The stereoselectivities exhibit a modest solvent dependence. Higher trans selectivities are observed with donor solvents (Table 2). For example, cyclopropanation of styrene catalyzed by Fe^{II}TTP yields a trans/cis ratio of 13:1 and 12:1 in THF and acetonitrile, respectively, whereas in dichloromethane the ratio of isomers is 8.8:1 and in toluene it is 8.0:1.

Cyclopropanation Using Fe(PFP)Cl. In order to simplify the system even further, we examined the cyclopropanation activity of iron *meso*-tetrakis(pentafluorophenyl)porphyrin chloride (Fe(PFP)Cl) in the absence of cobaltocene. We reasoned that if common porphyrins could be reduced by EDA at elevated temperatures, then perhaps this much more electron-deficient porphyrin would be transformed in situ to the Fe(II) species even at room temperature. Indeed, Fe(PFP)Cl catalyzed the cyclopropanation of various olefins by EDA efficiently at room temperature without the need for added cobaltocene. For example, over 4000 catalyst turnovers were observed in 6 h using styrene as the substrate (Table 1). This contrasts with Fe(TPP)Cl-catalyzed reactions which needed to be heated to 40 °C to effect reduction and subsequent cyclopropanation, or Fe(TMP)Cl-mediated reactions, which proceeded only at 80 °C (data not shown). In both cases, catalyst efficiency was much lower than that obtained with the Fe(PFP)Cl catalyst at room temperature. Although the stereoselectivity for the trans isomer (6:1 for styrene in dichloromethane) is slightly lower than that observed using conventional porphyrins in the cobaltocene-

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Table 1. Catalytic Cyclopropanation of Olefins with Ethyl Diazoacetate Using Iron Porphryin Complexes as Catalysts

olefin	catalyst[a]	reacton time (h)	t.o.n.[b]	ratio of trans/cis products[d]	ratio of cyclopropane/ diethyl maleate products
styrene	Fe(PFP)Cl	6	4200	6.0	75:25
	Fe(TPP)Cl/40 °C	10	400	5.5	76:24
	Fe(TPP)Cl/$CoCp_2$	2	910	8.7	80:20
	Fe(TTP)	1	1300	8.8	*e*
	Fe(TPP-*p*-OMe)Cl/$CoCp_2$	3	730	9.0	*e*
	Fe(TMP)Cl/$CoCp_2$	2	890	13	*e*
	Fe(OEP)Cl/$CoCp_2$	4	300	10	*e*
α-methylstyrene	Fe(PFP)Cl	3	4300	1.1	67:33
	Fe(TPP)Cl/40 °C	18	250	3.4	70:30
	Fe(TMP)Cl/$CoCp_2$	8	900	3.0	97:3
	Fe(OEP)Cl/$CoCp_2$	4	1800	3.7	85:15
	Fe(TTP)	1	1700	4.2	*e*
p-methoxystyrene	Fe(PFP)Cl	7	2000	5.8	*e*
	Fe(TPP)Cl/40°C	5	73	5.5	*e*
	Fe(TMP)Cl/$CoCp_2$	3	1400	11	*e*
ethyl vinyl ether	Fe(PFP)Cl	4	1800[c]	3.3	67:33
	Fe(TMP)Cl/$CoCp_2$	4	550[c]	4.1	82:18
	Fe(OEP)Cl/$CoCp_2$	4	250[c]	4.5	34:66
2-ethyl-1-butene	Fe(PFP)Cl	2	390		30:70

[a] 0.02−0.05% catalyst. [b] T.o.n. = turnover number, based on equivalents of cyclopropyl ester produced. Determined by GC unless noted otherwise. [c] Determined by ^1H NMR. [d] Determined by GC. [e] Trace diethyl maleate observed.

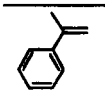
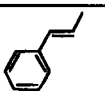
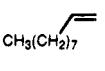
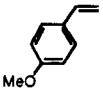
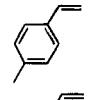
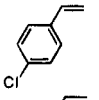
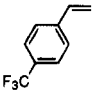
Table 2. Effect of solvent on cyclopropyl ester product isomer ratio in cyclopropanation reactions of styrene with EDA using [Fe(TTP)] as the catalyst

solvent	ratio of trans/cis products	solvent	ratio of trans/cis products
toluene	8.0	acetonitrile	12
benzene	8.3	ether	9.3
THF	13	styrene	8.3
dichloromethane	8.8		

initated reaction, it is still very good compared to commonly employed cyclopropanation catalysts. Moreover, Fe(PFP)Cl is commercially available.

Iron Porphyrin-Catalyzed Cyclopropanation Reactions Exhibit Pronounced Shape and Electronic Substrate Preferences. The iron porphyrins catalyzed the cyclopropanation of 1-alkenes and 1,1-disubstituted olefins very efficiently, but alkenes with other substitution patterns were poor substrates. Styrene, α-methylstyrene, and ethyl vinyl ether were cyclopropanated with reasonable to high efficiencies (Table 1), but only very low yields (less than 5%) of cyclopropane products were observed for *cis*- or *trans*-β-methylstyrene, indene, and 1-methylcyclohexene using Fe(PFP)Cl as the catalyst precursor (data not shown). This selectivity is borne out in competition studies. For example, when equal amounts of styrene and indene were mixed with limiting EDA in the presence of 0.035% Fe(PFP)Cl, a 26:1 ratio of styrene-derived to indene-derived cyclopropyl esters was obtained (Table 3). This is a remarkable example of shape selectivity in that these substrates differ by only a single methylene group. Trans-1,2-disubstituted alkenes are also poor substrates. Using Fe(TTP) as the catalyst, no detectable cyclopropanation products from *trans*-β-methylstyrene were detected in a competition experiment when equal amounts of *trans*-β-methylstyrene and α-methylstyrene were used as the substrates (Table 3). When *trans*-β-methylstyrene or cyclohexene alone was the substrate, diethyl maleate and fumarate were the only detectable products (data not shown). This shape selectivity is reminiscent of that observed for Os(TTP)-catalyzed cyclopropanation,[12] but contrasts with the much broader substrate compatibility of rhodium porphyrin-catalyzed reactions.[10] In the latter case, only tetrasubstituted alkenes are sluggish substrates.

Table 3. Competition experiments reveal significant electronic and shape preferences in the iron porphyrin-catalyzed cyclopropanation reactions

Olefin A	Olefin B	Catalyst	Ratio of Products Derived From A/B
		Fe(TTP)	only reaction of A observed
		Fe(PFP)Cl	26
		Fe(PFP)Cl	74
		Fe(TTP)	2.50
		Fe(TTP)	1.85
		Fe(TTP)	1.33
		Fe(TTP)	0.62
		Fe(TTP)	3.00

The iron porphyrin catalysts also exhibit pronounced preferences based on the electronic nature of the alkene. In general, olefins with aromatic or π-donating heteroatoms are better substrates. For example, 1,1-disubstituted alkenes with two alkyl substituents, such as 2-ethyl-1-butene, could be cyclopropanated, but yields were low due to a competitive reaction which formed diethyl maleate in high yield (Table 1). This product is presumably formed by the attack of EDA on the iron carbene, which will be favored if carbene transfer to the alkene is sluggish. The preference for aromatic substituents was also reflected in a competitive experiment in which equal amounts of styrene and 1-decene were present. Using Fe(PFP)Cl as the

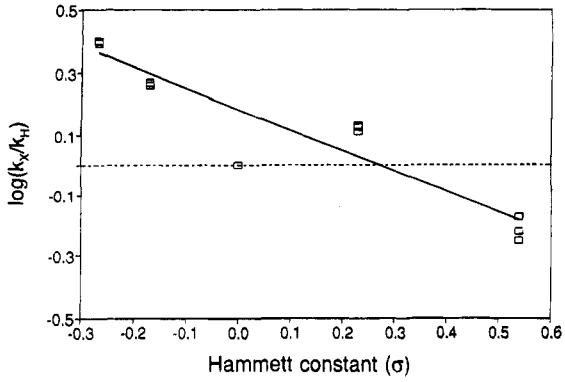


Figure 2. Hammett plot for the cyclopropanation of styrenes with EDA using Fe(TTP) as the catalyst.

catalyst, styrene was cyclopropanated at least 74 times more rapidly (Table 3).

A linear free energy relationship was derived from relative rate studies. Four cyclopropanation competition experiments were conducted with equimolar amounts of styrene and 4-X-styrene (X = OCH_3, CH_3, Cl, CF_3) and limiting quantities of EDA. Electron-donating substituents increased the rate of cyclopropanation, while electron-withdrawing substituents resulted in slower rates (Table 3). The data were fit to a Hammett plot (Figure 2) with $\varrho = -0.68 \pm 0.07$. Analogous electronic preferences were not observed in the corresponding rhodium poprhyrin-catalyzed cyclopropanation reactions,[15] suggesting that there is some buildup of electron deficiency on the alkene carbons in the transition state for carbene transfer from iron to the substrate, whereas this is not the case when rhodium porphyrins are employed. The electronic preferences exhibited by the iron porphyrin catalysts are similar to those observed for cyclopropanations catalyzed by $Os_2(TTP)_2$, again demonstrating the similarity between the iron- and osmium-based systems.

Isotope Effects. In order to probe the nature of the transition state of the iron-mediated cyclopropanation, the secondary kinetic isotope effect was determined in a competitive reaction between styrene and styrene-d_8 using Fe(PFP)Cl as the catalyst. A modest, but significant, inverse isotope effect of 0.87 ± 0.07 was observed. This suggests that there is some rehybridization of the olefin in the transition state of the iron-mediated reaction. In an analogous study using Rh(TMP)Me as the catalyst, no kinetic isotope effect was obeserved ($k_H/k_D = 1.0 \pm 0.07$).[15] Therefore, the transition state of the iron porphyrin-catalyzed reaction is later and more product-like than that of the rhodium-mediated reaction (see Discussion below).

Discussion

We have demonstrated that iron porphyrins can efficiently catalyze the cyclopropanation of alkenes. Exceedingly high turnover numbers have been observed and synthetically useful ratios of trans to cis cyclopropyl ester products were obtained. The trans to cis product ratios are comparable to the highest ratios observed for styrene, and those observed for α-methylstyrene and ethyl vinyl ether are the highest such ratios reported to date. The reaction also exhibits novel substrate preferences that depend on both the shape and electronic nature of the alkene. A variety of iron porphyrins, many of which are commercially available, have been shown to be effective catalysts.

Preformed iron(II) porphyrins are highly active catalysts, but are less convenient for use in most laboratories since they are extremely air-sensitive. Stable, easily handled iron(III) porphyrins can be employed as precatalysts if reduced in situ to generate the catalytically active iron(II) species. EDA, the carbene source, can itself act as the reductant. For common porphyrins, this requires that the solution be heated to 40−80 °C, which reduces the level of trans selectivity. This can be avoided by the addition of cobaltocene, which smoothly effects reduction of the precatalysts even at room temperature. Alternatively, Fe(PFP)Cl may be employed in the absence of cobaltocene at room temperature. Presumably, the electron-withdrawing pentafluorophenyl groups render the iron porphyrin more easily reduced by EDA. Very high turnover numbers and useful diastereoselectivities are observed using Fe(PFP)Cl as the precatalyst. Furthermore, this complex is commercially available, making the Fe(PFP)Cl-based system perhaps the most convenient for synthetic purposes.

We presume that the active intermediate in the iron porphyrin-catalyzed reactions is an iron carbene species formed by reaction of the iron(II) porphyrin with EDA. This is by analogy to earlier work in which we demonstrated that isolated, isoelectronic osmium(II) porphyrin carbene complexes are catalytically active.[12] In addition, we have presented evidence that rhodium porphyrin-catalyzed reactions proceed via an isoelectronic, cationic rhodium(III) carbene complex, although this species has eluded direct detection.[11] Although iron(II) carbene complexes have been reported previously,[16] none have been reported to be catalytically active for cyclopropanation. However, all of these isolated iron porphyrin carbene complexes were disubstituted, many with heteroatoms attached directly to the carbene carbon, and thus do not closely resemble the iron carbene complex relevant to our system.

The results presented here, combined with those obtained previously using osmium and rhodium porphyrin catalysts, illustrate the strong metal dependence of the diastereoselectivity and substrate preferences exhibited in porphyrin-mediated cyclopropanation reactions. The neutral osmium(II) and iron(II) catalysts provide the trans cyclopropyl ester as the major product and the influence of the groups appended to the porphyrin macrocycle is quite modest. Aryl or heteroatom-substituted alkenes are cyclopropanated much more efficiently than aliphatic alkenes, and only monosubstituted and 1,1-disubstituted alkenes are good substrates. The rhodium porphyrin-catalyzed reaction has strikingly different properties. Almost equal amounts of the cis and trans products are obtained with sterically unencumbered porphyrin ligands, but when bowl-shaped ligands such as TMP are employed, synthetically useful excesses of the cis product are produced. Furthermore, these reactions exhibit a very broad substrate compatibility. The electronic nature of the alkene substituent has little or no effect and only bulky tetrasubstituted alkenes are cyclopropanated inefficiently. The only exception is when the alkene substituents are very large. In these cases, monosubstituted alkenes are the preferred substrates.

These very significant differences are somewhat surprising in light of the fact that the putative osmium, iron, and rhodium carbene intermediates are isoelectronic. We propose here a model to reconcile these facts. The central tenet of this model is that transfer of the carbene ligand from the metal to the alkene proceeds along a similar reaction coordinate in each case, but

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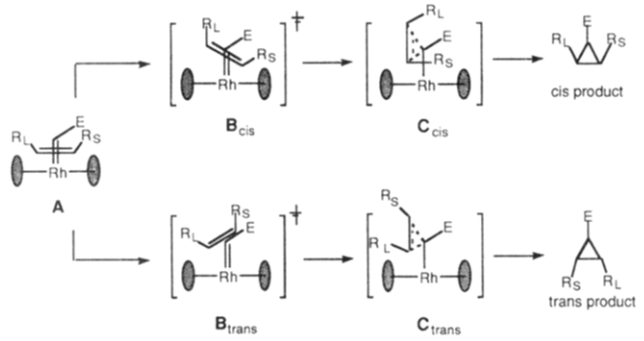

Figure 3. Proposed mechanism for the rhodium porphyrin-catalyzed cyclopropanation of alkenes. The porphyrin macrocycle is represented by the horizontal line, and meso-aryl substituents are represented by solid ovals. R_L = larger olefin substituent, R_S = smaller olefin substituent. An early transition state (structures **B**) is proposed. For steric reasons, $\mathbf{B}_{cis}$ is proposed to be preferred over $\mathbf{B}_{trans}$ when porphyrins with bulky meso substituents are employed.

that the transition state is very early in the rhodium-catalyzed reaction but relatively late in the iron and osmium-mediated reactions.

We have previously proposed the scheme for carbene transfer from rhodium porphyrins to an alkene shown in Figure 3.[15] The substrate is envisioned to approach the metallocarbene in a roughly perpendicular orientation relative to the metal−carbon axis and then to rotate either clockwise (Figure 3, top pathway) or counterclockwise (Figure 3, bottom pathway), eventually reaching the arrangement of atoms found in the product. These pathways would eventually lead to the cis and trans cyclopropyl esters, respectively. We assume that the largest alkene substituent would approach so as to avoid the ester group. Since the rhodium(III)−carbene complex is exceedingly electrophilic and because the reaction does not display a detectable secondary isotope effect, the transition state for carbene transfer ($\mathbf{B}_{cis}$ and $\mathbf{B}_{trans}$ in Figure 3) is likely to be very early. This is consistent with the absence of a secondary isotope effect and also rationalizes the observed substrate selectivity. Only in cases of extremely bulky substituents or tetrasubstituted alkenes do the substrates suffer severe steric interactions with the catalyst. Furthermore, if there is no significant polarization of the olefinic carbons, then substituent effects should be very modest, which is the case. Finally, as the porphyrin becomes more bowl-shaped, the transition state leading to the trans product will be increasingly destabilized relative to that leading to the cis product, since R_L, the larger substituent, must rotate toward the peripheral porphyrin substituent (solid oval). Many other observations are also consistent with this model.

In contrast, we propose that in the iron and osmium systems, the transition state for carbene transfer is reached later and resembles species **C** in Figure 4. This seems reasonable based on the fact that the iron(II) and osmium(II) carbenes should be less electrophilic than the Rh(III) species. Indeed, osmium(II) carbenes are isolable at room temperature, while rhodium(III) carbenes are highly reactive even at low temperatures. The later transition state postulated in Figure 4 implies that the alkene carbons should have some carbocationic (or radicaloid) character and should no longer be completely sp^2-hybridized, though it is far from a full-blown carbonium ion. This is consistent with the observation of a modest negative ϱ value in the Hammett plot and the small inverse secondary deuterium isotope effect. It also rationalizes why aromatic alkenes and enol ethers are superior substrates. In addition, the orientation of the alkene with respect to the porphyrin plane would strongly select against the presence of substituents on the carbon closest to the macrocycle, thus explaining the pronounced shape selectivity

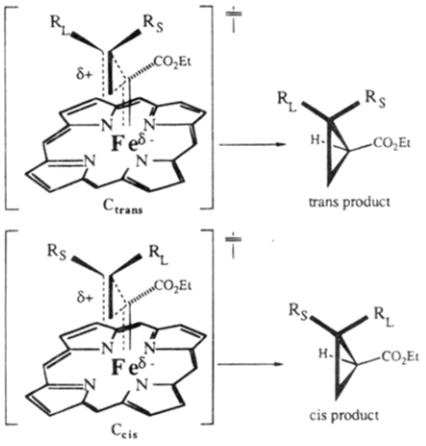

Figure 4. Proposed transition state for iron porphyrin-catalyzed cyclopropanation reactions. The porphyrin meso substituents were omitted for clarity. R_L = larger olefin substituent, R_S = smaller olefin substituent. A later transition state than in the rhodium porphyrin-catalyzed reaction is proposed in which the olefin is parallel to the metallocarbene and significant bond forming has occurred (structures **C** which are analogous to the corresponding structures **C** in Figure 3). This geometry rationalizes why 1,2-disubstituted alkenes are poor substrates, since one of the alkene substituents would suffer severe steric interactions with the porphyrin macrocycle. $\mathbf{C}_{trans}$ is proposed to be preferred over structure $\mathbf{C}_{cis}$ since this minimizes steric interactions between the carbene ester and the larger alkene substituent.

observed. Finally, since the alkene substituents R_L and R_S project up and out of the porphyrin pocket one would not predict that the groups appended to the porphyrin would have a large effect on the stereochemical outcome of the reaction. Rather, this would be dominated by the interaction between R_L and the ester, leading to the trans product. This is in agreement with the observation that many different porphyrins provide similar trans/cis product ratios for a given alkene, and that the modest differences observed do not correlate with the steric bulk of the porphyrin substituents (Table 1). Another appealing aspect of the model is that it rationalizes why donor solvents slightly increase the trans to cis product ratio. If the trans preference is the result of a late transition state, which in turn is due to the relatively modest electrophilicity of the metallocarbene, then an axially ligated donor solvent should make the carbene even less electrophilic. This model will be employed as the basis for the rational design of enantioselective porphyrin cyclopropanation catalysts.

Experimental Section

General Procedures. Dichloromethane and acetonitrile were distilled from calcium hydride suspension before use. THF, diethyl ether, benzene, and toluene were distilled from sodium benzophenone ketyl. Olefins, decane, and tridecane were purchased from Aldrich and were passed through a plug of alumina and degassed with argon before use. Ethyl diazoacetate, Fe(PFP)Cl, Fe(TPP)Cl, and Fe(TPP-*p*-MeO)-Cl were purchased from Aldrich and used as received. Tetramesitylporphyrin was prepared according to the method of Lindsey.[17] Fe(TMP)Cl was prepared by reaction of TMP with excess $FeCl_2$ in refluxing DMF for 12 h, followed by precipitation into 1 M HCl according to the procedure of Kobayashi.[18]

All reactions with Fe(TTP) were carried out under a nitrogen atmosphere using a Vacuum/Atmospheres glovebox equipped with a model MO40DH DriTrain gas purification system. Solvents and reagents used in the Fe(TTP) reactions were degassed by 3 freeze−pump−thaw cycles. Fe(TTP) was synthesized using the procedure of Reed by reduction of either Fe(TTP)Cl or $[Fe(TTP)]_2(\mu\text{-O})$ with Zn/

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Hg amalgam in THF for 12 h.[19] The UV/vis spectrum for Fe(TTP) was analogous to that of other iron(II) porphyrins.[20]

The stereochemistry of the cyclopropyl ester products was assigned by ^{1}H NMR spectroscopy by comparison with published data.[12,21] Once the major isomer was assigned by ^{1}H NMR, product ratios were determined by GC.

Cyclopropanation Reactions Using Fe(TTP). In a typical experiment, 2.9 mg (4.0×10^{-6} mol) of Fe(TTP), 8.7×10^{-3} mol of olefin, and 22.5×10^{-6} L (16.8 mg) of dodecane (internal GC standard) were placed into a round-bottom flask and dissolved in 3 mL of solvent. A solution of ethyl diazoacetate (90 μL, 860×10^{-6} mol) in 12 mL of solvent was added dropwise over approximately 1 h to the solution of catalyst and olefin with vigorous stirring. After the addition was finished, an aliquot of the reaction mixture was taken and diluted 4-fold with fresh solvent. The solution was analyzed by gas chromatography to determine the yield of the reaction. To achieve maximum turnover numbers, aliquots of EDA were added to the porphyrin and substrate-containing solution (10 mL of toluene with dodecane as an internal standard) until no further reaction was observed.

Cyclopropanation Reactions Using Iron(III) Porphyrins Reduced in Situ. In a typical reaction, the iron(III) porphyrin complex (1.8×10^{-6} mol) and cobaltocene (2×10^{-5} mol) were placed in a round-bottom flask which was then evacuated and back-filled with argon. Dichloromethane (5 mL) was then added, followed by degassed olefin (9.4×10^{-3} mol) and decane (0.200 mL, 1.0×10^{-3} mol) or (0.200 mL, 8.2×10^{-4} mol) tridecane as an internal GC standard. The flask was placed in a room temperature water bath. An oil bubbler line was attached to the flask and the argon line removed. The first aliquot of EDA (0.10 mL, 9.5×10^{-4} mol) was added to initiate the reaction. In the cases of high catatyst activity, vigourous bubbling was observed within 2 min, and additional aliquots of EDA were added at approximately 15-min intervals until bubbling ceased. In the cases where no reaction was observed immediately, the water bath was replaced with a heating mantle and the reactions were heated to reflux temperature (no additional EDA was added). In all cases cyclopropane formation was monitored by GC.

Competition Studies Using Fe(PFP)Cl. These experiments were performed in a manner analgous to those described above, using equimolar amounts of each olefin (approx. 9.4×10^{-3} mol each) and 0.035% Fe(PFP)Cl (based on total olefin) in a room temperature water bath. The product ratios listed in Table 3 were determined at early time points in the reaction (15 min, 0.2 equiv of EDA added based on total olefin).

Competition Studies Using Fe(TTP). In a typical experiment Fe(TTP) (2.0 mg, 2.8×10^{-6} mol), 7.6×10^{-3} mol of each olefin, and dodecane (0.0225 mL, 9.86×10^{-5} mol) were placed in a round-bottom flask and dissolved in 15 mL of toluene. EDA (0.040 mL, 3.8×10^{-4} mol) was added with vigorous stirring. GC analysis was then performed to determine yields.

Determination of the Secondary Kinetic Isotope Effect k_H/k_D. Equimolar amounts of styrene and styrene-d_8 (0.050 mL, 4.4×10^{-4} mol each) and Fe(PFP)Cl (2.0 mg, 1.8×10^{-6} mol) were dissolved in dichloromethane (3 mL) in a round-bottom flask. The solution was deoxygenated by 3 freeze–pump–thaw cycles, and was backfilled with argon. The flask was placed in a room temperature water bath. An oil-bubbler line was attached to the flask and the argon line removed. EDA (0.035 mL, 2.8×10^{-4} mol) was added over a period of 20 min, after which time the solution was allowed to stir for an additional 0.5 h. The reaction mixture was analyzed by GC-MS (Finnegan 4500 ITD) in selected ion monitoring mode (detecting masses 190 and 198), and the peak areas were integrated and corrected for the k_H/k_D of ionization. The observed secondary kinetic isotope effect was 0.87 ± 0.07 and represents the average of at least 5 GC-MS runs each of three reactions.

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